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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,383	09/08/2003	Yan Chang	GLYO-P03-002	9375

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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/657,383	CHANG ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-5 and 7-28 are pending. Any objection or rejection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 4 and 23-28 are again rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, as set forth in the previous Office action. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that Applicant, at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed August 15, 2006 have been fully considered but they are not persuasive.

Applicant contends that support for these claims resides in S. N. 09/750,726 (now US 6,423,314), which shows oligomeric or polymeric species having dependent side chains of one or more sugars such as galactose or arabinose. A particular embodiment has a cellulose backbone with dependent galactose terminated side chains. This embodiment is depicted in Fig. 4 of the reference. The reference further describes this embodiment as material comprising lactose bound to a polymer chain. The embodiment is a cellulose-based polymer. This embodiment would support a limitation for a "cellulose-based polymer." There is no indication that the

homopolymeric structure of the backbone is a critical element that may be extrapolated to support this generic limitation.

Applicant further notes that the present specification shows a group of materials with a "substantially demethoxylated polygalacturonic acid backbone and dependent rhamnose residues and side chains having terminal glucose [sic – galactose?] and arabinose units dependent from the backbone." First of all, the examiner agrees that the specification discloses two particular polyGalA embodiments (structure I). However, it is not clear what Applicant means by "demethoxylated polygalacturonic acid backbone and *dependent rhamnose residues*." Is it Applcant's position that the rhamnose moieties in structures II and III are *not* in the backbone? The examiner interprets these structures as having alternating galacturonic acid and rhamnose moieties making up the backbone of the polymeric material. These two embodiments would support limitations wherein the backbone comprises "alternating galacturonic acid and rhamnose moieties" or "polyGalA" with arabinose and/or galactose (not glucose) branches, not a generic homopolymer or a generic polymer with side chains being terminated by a galactose or arabinose.

Applicant further contends that the specification discloses pectin, which is a polygalacturonic backbone with number side chains with rhamnose residues. Again, this does not support generic branching.

Further regarding the limitation "homopolymer," Applicant contends that the specification provides "numerous examples" of homopolymers. In fact, the specification discloses two (out of four) specific embodiments having polygalacturonic backbones. Applicant contends that one of ordinary skill would have recognized both formulas I and II as

homopolymers. The examiner agrees that one of ordinary skill would recognize formula I as a homopolymer. However, one of ordinary skill would recognize formula II as a polymer having alternating galacturonic acid and rhamnose units. Even though formula I is clearly a polymer that happens to have a homopolymeric backbone, this example does not clearly support a limitation to a generic homopolymer.

The examiner maintains that these specific embodiments do not support the generic limitations recited in the claims.

Claim Rejections - 35 USC § 103

Claims 1-4, 7, 13 and 18-28 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Klyosov et al (US 6,645,946), as set forth in the previous Office action.

Klyosov '946 teaches the administration of galactomannan and 5-FU by injection to mice. See examples. It is noted that the mice in the examples do not actually have cancer. The reference also describes the structure of galactomannan. See paragraph bridging col 5-6. This structure appears to meet the criteria of carbohydrates that would bind to galectin-1 or galectin-3.

Although the reference does not exemplify administration to a patient having cancer, the reference specifically suggests the administration of the galactomannan/chemotherapeutic agent as a treatment for cancer. See col 2, lines 15-65. The reference teaches that the administration of the galactomannan reduces side effects produced by toxic chemotherapeutic agents. See abstract. The reference further suggests a variety of modes of administration, including oral, and sequential administration of the galactomannan and chemotherapeutic agent. See col 3, lines 35-

55, and col 4, lines 41-43 and reference claim 16. The reference is silent regarding radiation or surgical treatment.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer galactomannan with an oncolytic chemotherapeutic in order to reduce side effects produced by the chemotherapeutic agent with a reasonable expectation of success. As noted above, the reference is silent regarding "enhanced efficacy." However, the same patient population would be treated, regardless of whether the intent was to reduce side effects or enhance efficacy. Recognition of another advantage that would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. In the absence of unexpected results, it would be within the scope of the artisan to determine the optimum mode of administration and protocol regarding the relative timing of administration of the components through routine experimentation. It would be further obvious to combine the galactomannan/chemotherapeutic treatment with other common treatments such as radiation or surgical. One of ordinary skill in the art would reasonably expect success in this combination because the use of chemotherapeutic agents in combination with radiation and/or surgery is common in the art of cancer treatment.

Applicant's arguments filed August 15, 2006 have been fully considered but they are not persuasive.

Applicant first notes that the administered dosages are not therapeutically effective in a cancer patient. However, this allegation is unsupported by evidence and is therefore unpersuasive.

Applicant further argues that there are no cancer patients in Klyosov, "so there can be no same patient population." The examiner respectfully disagrees. The reference expressly suggests the combination of galacotmannan in combination with chemotherapeutic agents to treat a variety of cancers. See col 2, lines 49-65. Cancer patients would be inherent in a method of treating cancer.

Applicant further contends that "efficacy refers to the minimum amount of a drug or treatment capable of obtaining a thereapeutic [sic] result," as if "efficacy" defined a particular dose. The examiner respectfully disagrees with this definition of efficacy. "Efficacy: power to produce effects or intended results; effectiveness." (See entry for "efficacy" *Webster's New World Dictionary*, third college edition, 1988.) Applicant goes on to discuss FDA clinical trials, but it is not clear how this discussion is relevant to the rejection. The examiner maintains that it would be obvious to combine galctomannan and a chemotherapeutic agent for the treatment of cancer based on Klyosov for reasons set forth above. Any increased efficacy would flow from the suggestions in Klyosov.

Applicant further argues that the reference fails to teach of suggest that galactomannan binds to any galectins. The carbohydrate disclosed in the reference appears to meet the structural requirements of a product that would bind a galectin. The burden is on Applicant to show that it does not have this property. The fact remains that the reference expressly suggests the combination of galacotmannan in combination with chemotherapeutic agents to treat a variety of cancers. Furthermore the fact that the reference does not recognize or discuss every possible inherent property of the carbohydrate does not make it any less obvious.

Finally, even though the reference does not mention surgery or radiation, the examiner maintains that it would be obvious to combine the galactomannan/chemotherapeutic treatment with other common treatments such as radiation or surgical as discussed above.

Claims 1-3, 13, 14 and 18-22 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al (Anti-Cancer Drug Design, 1999), as set forth in the previous Office action.

Green teaches as set forth in the previous Office action. The reference does not exemplify the full range of therapeutic treatments recited in the claims. However, the reference does suggest the use of the antimetastatic glycoamines in combination with traditional therapies. See, for example, section "Anti-adhesives as chemosensitizers for ascites tumors" at page 157.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer a disclosed glycoamine in combination with any traditional therapy. It would be within the scope of the artisan to select any known therapy, such as those recited in the claim. One of ordinary skill would be motivated to combine these methods of treatment for their additive effects with a reasonable expectation of success. In preventing metastasis, the addition of the glycoamine would clearly enhance the efficacy of any other treatment. In the absence of unexpected results, it would be within the scope of the artisan to optimize the treatment protocol with respect to the timing and mode of administration through routine experimentation.

Applicant's arguments filed August 15, 2006 have been fully considered but they are not persuasive.

Applicant first discusses the reference's teaching regarding the use of 4-HC and bovine testicular hyaluronidase on mouse and human cells. This is an interesting result, but has no relevance to the rejection, which is based on the use of the carbohydrate products, the glycoamines.

Applicant further contends that the reference shows only *in vitro* experiments and does not suggest *in vivo* experiments, treatment of cancer patients or the administration of a galectin-binding carbohydrate in combination with surgery or radiation treatment. The examiner respectfully disagrees. In a passage cited in the previous Office action, the reference states: "Additional experiments are currently underway in our laboratory to determine the ability of synthetic glycoamine analogues to increase the efficacy of chemotherapy *in vivo*, as well as examining any potentially synergistic effects with other chemotherapeutic agents and/or radiation therapy in ovarian carcinoma and other tumor systems." See paeg 161, 1st full paragraph. The inherent property of galectin-binding is addressed above.

Claims 1-3, 12, 13 and 18-22 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Rubin et al (US 5,639,737), as set forth in the previous Office action.

Rubin teaches that lactose or lactose conjugates of chemotherapeutic agents inhibit tumor growth and metastasis. See abstract. The reference suggests the administration of lactose or a conjugate to prevent metastases resulting from surgery, with the lactose or conjugate being administered beginning 8-12 hours prior to surgery and continuing for 3 days post-operatively. See col 14, lines 27-31.

The reference also suggests the administration of lactose alone or in combination with a lactose conjugate. See, for example, col 16, lines 33-38. In the latter case, the free lactose would correspond to the galectin-binding carbohydrate, and the conjugate would correspond to the oncolytic chemotherapeutic. The reference further suggests the combination with other treatments. See col 17, lines 8-23. The reference is silent regarding galectin-binding, but it appears to meet the physical characteristics in that it comprises a galactose moiety, and has a molecular weight greater than the minimum contemplated.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer lactose in combination with surgery or in combination with a chemotherapeutic lactose conjugate for the treatment of cancer. One of ordinary skill would be motivated to combine these methods of treatment for their additive effects with a reasonable expectation of success. In preventing metastasis, the addition of the lactose would clearly enhance the efficacy of the surgical or chemotherapeutic treatment. In the absence of unexpected results, it would be within the scope of the artisan to optimize the treatment protocol with respect to the timing and mode of administration through routine experimentation.

Applicant's arguments filed August 15, 2006 have been fully considered but they are not persuasive.

Applicant's only argument appears to be that the reference does not teach that lactose binds galectin. This issue is addressed above. The burden remains on Applicant to demonstrate that lactose does not bind galectin.

Claims 1-5, 7-9, 12, 13 and 15-28 are again rejected under 35 U.S.C. 103(a) as being unpatentable over either of (1) Green et al (Anti-Cancer Drug Design, 1999) or (2) Rubin et al (US 5,639,737) in view of Platt et al (WO 97/34907), as set forth in the previous Office action.

Each of Green and Rubin teach the use of antimetastatic agents in combination with standard treatments for cancer. Neither reference teaches the use of modified pectin in combination with other therapeutic treatments for cancer.

Platt teaches that modified citric pectin (MCP) with molecular weight of about 10 kD has utility in the treatment and prevention of metastatic cancer. See pages 1-3 and page 6, lines 2-6.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer MCP in combination with any traditional cancer treatment. Each of Green and Rubin had taught the use of antimetastatic agents in combination with standard treatments for cancer. Therefore, one of ordinary skill would reasonably expect success in using this combination for the additive effect.

Applicant's arguments filed August 15, 2006 have been fully considered but they are not persuasive.

Applicant first objects to the non-use of particular words in Platt. If all these words had been used, the rejection might have been one of anticipation rather than one of obviousness. However, Platt teaches that modified citric pectin (MCP) with molecular weight of about 10 kD has utility in the treatment and prevention of metastatic cancer, as discussed above.

This issue of galactose-binding is addressed above. The burden remains on Applicant to demonstrate that the modified citrus pectin disclosed by Platt does not bind galectin. The fact

that this property is not disclosed does not negate the teaching regarding the treatment of metastasis, known in the art to be a frequent occurrence in cancer.

Applicant notes that Green (1999) fails to cite Platt (1997), and neither of Green nor Platt cites Rubin (1997). In is unclear how these non-citations negate the appropriateness of the combination of references. As noted above, Green, for example, expressly suggests the combination of the disclosed glycoamines with other chemotherapeutic agents. It also appears that Green fails to cite every reference concerning every chemotherapeutic agent that was known in 1999.

In response to Applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the reason was clearly stated in the previous Office action: Each of Green and Rubin had taught the use of antimetastatic agents in combination with standard treatments for cancer. Therefore, one of ordinary skill would reasonably expect success in using the Platt product in the same manner for the additive effect.

In response to Applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the

time the claimed invention was made, and does not include knowledge gleaned only from the Applicants disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Claims 1-5, 7-10, 12, 13 and 15-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of (1) Green et al (Anti-Cancer Drug Design, 1999) or (2) Rubin et al (US 5,639,737) in view of Platt et al (WO 97/34907) and further in view of Ros et al, (Carbohyd. Res., 1996).

Green, Rubin and Platt teach as set forth above. Platt teaches the use of pH modified MCP but also specifically suggests that the citrus pectin may be modified by methods and experimental conditions known in the art may be used to prepare the MCP. See paragraph bridging pp 6-7. The reference does not exemplify citrus pectin modified enzymatically.

Ros teaches the enzymatic hydrolysis of pectin. See pp 272-3.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use any method, such as enzymatic, known in the art to depolymerize pectin to arrive at the MCP having anti-metastatic activity for use in the method made obvious, as set forth above. Platt had taught the general physical requirements and suggested the use of other methods. Therefore it would be within the scope of the artisan to use the method taught by Ros to prepare an appropriate product through routine experimentation with a reasonable expectation of success.

Applicant's arguments filed August 15, 2006 have been fully considered but they are not persuasive.

Applicant also objects to Ros's non-use of particular words and non-identification of pectin as a galactin-binding product. These points are addressed above. Applicant's allegation of hindsight reasoning in also addressed above.

Applicant further contends that Ros is non-analogous art, as it has nothing to do with the treatment of cancer. "In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be *reasonably pertinent to the particular problem with which the inventor was concerned.*" (emphasis added) In re Oetiker, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). See also In re Deminski, 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986); In re Clay, 966 F.2d 656, 659, 23 USPQ2d 1058, 1060-61 (Fed. Cir. 1992) ("A reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's endeavor, it is one which, *because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem.*"); (emphasis added) Wang Laboratories Inc. v. Toshiba Corp., 993 F.2d 858, 26 USPQ2d 1767 (Fed. Cir. 1993); and State Contracting & Eng 'g Corp. v. Condotte America, Inc., 346 F.3d 1057, 1069, 68 USPQ2d 1481, 1490 (Fed. Cir. 2003) (where the general scope of a reference is outside the pertinent field of endeavor, the reference may be considered analogous art if subject matter disclosed therein is relevant to the particular problem with which the inventor is involved). In the instant case, Ros is drawn to the preparation of modified pectin. A reference drawn to a manipulation of pectin in such a way that does not make it unsuitable for use in cancer treatment is reasonably analogous art.

Claims 1-5, 7-9, 11-13 and 15-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of (1) Green et al (Anti-Cancer Drug Design, 1999) or (2) Rubin et al (US 5,639,737) in view of Platt et al (WO 97/34907) and further in view of Renard et al, (Carbohyd. Res., 1995).

Green, Rubin and Platt teach as set forth above. Platt teaches the use of pH modified MCP but also specifically suggests that the citrus pectin may be modified by methods and experimental conditions known in the art may be used to prepare the MCP. See paragraph bridging pp 6-7. The reference does not exemplify citrus pectin modified thermally.

Renard teaches the thermal hydrolysis of pectin. See pp 156-7, section 2.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use any method known in the art, such as thermal, to depolymerize pectin to arrive at the MCP having anti-metastatic activity for use in the method made obvious, as set forth above. Platt had taught the general physical requirements and suggested the use of other methods. Therefore it would be within the scope of the artisan to use the method taught by Renard to prepare an appropriate product through routine experimentation with a reasonable expectation of success.

Applicant's arguments filed August 15, 2006 have been fully considered but they are not persuasive.

Applicant also objects to Renard's non-use of particular words and non-identification of pectin as a galactin-binding product. These points are addressed above. Applicant's allegation of hindsight reasoning in also addressed above.

Applicant further contends that Renard is non-analogous art, as it has nothing to do with the treatment of cancer. In the instant case, Renard is drawn to the preparation of modified pectin. A reference drawn to a manipulation of pectin in such a way that does not make it unsuitable for use in cancer treatment is reasonably analogous art. See discussion of analogous art, as it applies to Ros, above.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
November 17, 2006